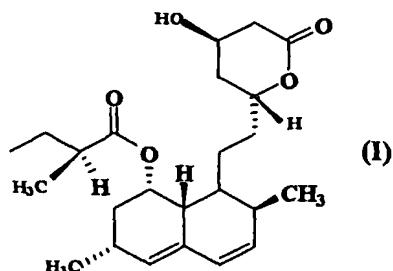


V

Claims:

1. A method for lactonisation and isolation of Lovastatin of formula (I):



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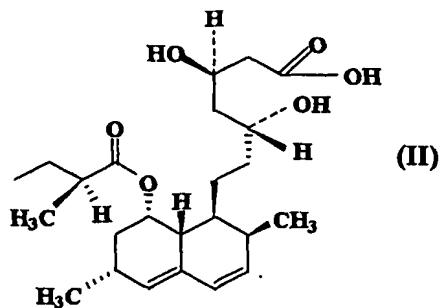
which comprises the steps of:

10 a) adjusting the pH of a fermentation broth containing mevinolinic acid (II) at 3.5 ± 0.1 with a mineral acid, and optionally filtering the fermentation broth,

b) adding a hydrophobic solvent to the aqueous fermentation broth or the mycelia cake and bubbling an inert gas into the biphasic mixture,

c) heating the fermentation broth or the mycelia cake at $55 \pm 5^\circ\text{C}$, in the presence of a hydrophobic solvent, carrying out lactonisation of mevinolinic acid (II) and extracting f Lovastatin (I) into a hydrophobic solvent, concurrently, in a time period between 12 - 19 hours, under constant nitrogen bubbling,

15 d) isolating impure Lovastatin (I) from said hydrophobic solvent,



20 e) purifying impure Lovastatin (I) by dissolving impure Lovastatin (I) in a chlorinated solvent followed by removal of suspended resinous impurities by filtration, adding a hydrophobic solvent, heating the mixture to $55 \pm 5^\circ\text{C}$, evaporating the chlorinated solvent followed by crystallization from a hydrophobic solvent to give pure Lovastatin (I), or by dissolving Lovastatin(I) in

a mixture of a chlorinated solvent and a hydrophobic solvent, filtering the suspended impurities, and heating the mixture to $55 \pm 5^\circ\text{C}$, followed by evaporating the chlorinated solvent and crystallizing from the hydrophobic solvent to give pure Lovastatin (I),

5 f) recrystallising Lovastatin (I), from an aliphatic alcohol, by heating Lovastatin (I) with an aliphatic alcohol between 65 to 75°C for 30 minutes, cooling the mixture between -5 to $+5^\circ\text{C}$ and filtering crystalline Lovastatin (I) followed by drying at 35 - 40°C to give pure Lovastatin (I), substantially free from impurities and conforming to pharmacopoeial specification.

10 2. A method as claimed in claim 1, wherein said pure Lovastatin is further purified by heating said pure Lovastatin in the presence of alumina in a water miscible solvent at a temperature in the range of 50 - 60°C , filtering the mixture and crystallizing extrapure Lovastatin(I) conforming to pharmacopoeial specification.

15 3. A method as claimed in claim 1, wherein said steps of lactonisation and concurrent extraction by a hydrophobic solvent are carried out in a time period of not more than 20 hours,

4. A method as claimed in any preceding claim 1, wherein the acid used for adjusting the pH is a mineral acid.

5. A method as claimed in claim 4, wherein said mineral acid is hydrochloric acid, sulphuric acid, nitric acid or orthophosphoric acid.

20 6. A method as claimed in any preceding claim 1, wherein said hydrophobic solvent is selected from aliphatic hydrocarbon, aromatic hydrocarbon, and chlorinated hydrocarbon.

7. A method as claimed in any preceding claim, wherein said lactonisation of mevinolinic acid (II) and extraction of Lovastatin (I) is carried out at a temperature in the range of 50 - 60°C ,

25 8. A method as claimed in any preceding claim wherein the inert gas bubbled in the reaction medium is selected from nitrogen, argon and helium.

9. A method as claimed in any preceding claim , wherein said chlorinated solvent required for dissolving impure Lovastatin (I) is selected from dichloromethane, 1,2-dichloroethane and chloroform.

10. A method as claimed in any preceding claim wherein said aliphatic alcohol employed for recrystallisation of Lovastatin (1) is isopropanol.
11. A method as claimed in claim 2, wherein the water miscible solvent is selected from ketonic solvent and an alcoholic solvent.
- 5 12. A method as claimed in claim 11, wherein said ketonic solvent is acetone.
13. A method as claimed in claim 12, wherein said alcoholic solvent is isopropanol.
14. A method as claimed in claim 2, wherein said alumina is selected from acidic alumina, basic alumina, neutral alumina.

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